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Dossier: Diabetes: basic research and clinical approach

Ineffectiveness of allopurinol in reduction of oxidative stress in diabetic patients; a randomized, double-blind placebo-controlled clinical trial

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Abstract

The objective of this randomized, double-blind placebo-controlled clinical trial was to evaluate the value of allopurinol treatment on reduction of oxidative stress in patients with diabetes type II patients. Forty-one diabetic type II subjects were randomly assigned to two groups. One group ($n = 20$) received 100 mg allopurinol three times a day for 14 days and the other group ($n = 21$) received a placebo. Blood and saliva samples were collected before and after intervention for analysis of lipid peroxidation level and total antioxidant power as indices of oxidative stress. At the beginning of the study, the groups were similar based upon age, duration of diabetes, fasting glucose, and HbA1c. Both allopurinol and placebo were effective in reduction of lipid peroxidation and total antioxidant power whether in saliva or plasma in a similar extent. HbA1c and FBS levels did not change through the study neither in case or placebo group. It is concluded that allopurinol therapy is not more effective than placebo in reduction of oxidative stress in diabetic patients. The same trend of changes in blood and saliva shown for oxidative stress indices was interesting and suggests a chance for saliva to be valuable in diagnosis of oxidative stress. However, to elaborate the exact role of allopurinol in diabetes, further large randomized clinical trials are needed.

Keywords: Diabetes; Allopurinol; Oxidative stress

1. Introduction

Reactive oxygen species (ROS) and disturbed antioxidant status have been reported in diabetes [1–4]. Occurrence of oxidative stress in diabetes is probably due to the abnormal metabolic milieu such as hyperglycemia, dyslipidemia and elevated free fatty acids (FFA), which commonly occur in diabetic patients [5–8]. In cultured vascular cells, elevating glucose levels in the media has been shown to enhance oxidant production including gluco-oxidants, glycated compounds, oxidized LDL, superoxidants, and nitrotyrosine [5,9–12]. Oxidative stress contributes to the development of microvascular (i.e. retinopathy and nephropathy) and cardiovascular diseases associated with diabetes type I and II [1–4]. In addition, oxidative stress has been suggested to cause abnormalities in secretion and action of insulin [13,14].

Thus, antioxidant therapy may prevent the main complications of diabetes. The beneficial effects of antioxidants, such as vitamin C, vitamin E, β-carotene, and lipoic acids have been reported in cultured vascular cell, animal models of diabetes and in patients with diabetes [15–20]. However, supportive evidence that antioxidants can provide beneficial effects in diabetes in clinical trials is lacking.

One of the main mechanisms of ROS production and atherosclerosis in diabetes is thought to be mediated by xanthine oxidase [21]. Xanthine oxidase, is formed from xanthine dehydrogenase through either proteolytic cleavage or by oxidation of cysteines. Both xanthine oxidase and xanthine dehydrogenase convert hypoxanthine to xanthine and of xanthine to uric acid. However, xanthine oxidase has the unique property of being able to reduce oxygen to form superoxide and hydrogen peroxide. Xanthine oxidase is

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